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10/005,907	12/07/2001	Karl Nocka	053529-5005	7080

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EXAMINER	
HUYNH, PHUONG N	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 05/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/005,907	NOCKA ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *2/4/04; 12/9/03; 7/23/02*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-71* is/are pending in the application.

4a) Of the above claim(s) *6-22,30-48 and 50-71* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,23-29 and 49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/10/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-71 are pending.

2. Applicant's election with traverse of Group 1, claims 1-5, 23-29 and 49, drawn to isolated nucleic acid, vector, host cell, and composition comprising said nucleic acid, filed 12/9/03, is acknowledged. However, because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Further, the request to rejoin process claims (claims 35-37, 39, 43-48 and 50-55) that once a product claim in Group 1 found to be allowable is acknowledged. However, it is noted that claims 36 and 37 are drawn to a method of identifying an agent which modulates at least one of activity of a protein instead of the expression of nucleic acid. These methods differ with respect to the method steps and endpoints. Therefore, claims 36 and 37 will not be rejoined with Group 1 if Group 1 is found to be allowable.

3. Claims 6-22, 30-48, and 50-71 are withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

4. Claims 1-5, 23-29 and 49 are being acted upon in this Office Action.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 3, 5, 23-29 and 49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for an isolated nucleic acid molecule comprising SEQ ID NO: 1 that encodes the amino acid sequence of SEQ ID NO: 2, the complement of SEQ ID NO: 1 that encodes the amino acid sequence of SEQ ID NO: 2, a vector and an isolated host cell comprising said nucleic acid molecule for detection of allergic hypersensitivity in a patient, **does not** reasonably provide enablement for *any* isolated nucleic acid molecule that encodes any fragment of at least 6 amino acids of SEQ ID NO: 2, any nucleic acid molecule which hybridizes to the complement of a nucleic acid molecule comprising SEQ ID NO: 1, any isolated nucleic

acid molecule which hybridizes to the complement of any nucleic acid molecule that encodes the amino acid sequence of SEQ ID NO: 2, any isolated nucleic acid molecule that encodes any protein that exhibits at least about 35% amino acid sequence identity to SEQ ID NO: 2, any isolated nucleic acid molecule "comprises" nucleotides 25-249 of SEQ ID NO: 1, any vector comprising the isolated nucleic acid molecule mentioned above, any "host cell" transformed to contain the nucleic acid molecule mentioned above, a method for producing a polypeptide comprising culturing a host cell transformed with the nucleic acid molecule mentioned above and a composition comprising any isolated nucleic acid molecules mentioned above and an aqueous carrier. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only an isolated nucleic acid molecule comprising SEQ ID NO: 1 that encodes the amino acid sequence of SEQ ID NO: 2, a vector and an isolated host cell comprising said nucleic acid molecule for producing said polypeptide. The specification further discloses that a change in the expression levels of said nucleic acid molecule is associated with allergic hypersensitivity in a patient. The specification discloses overexpression of polynucleotide reduces the release of degranulation as determined by marker β hexoseaminidase, decreases the release of PGD2, LTC4, and GM-CSF 18 hours after activation.

The specification does not teach how to make any nucleic acid molecule mentioned above because there is insufficient guidance as to the structure without the nucleotide sequence of all nucleic acid molecule that encodes which 6 amino acids of SEQ ID NO: 2, so long the nucleic acid encodes 6 amino acids of SEQ ID NO: 2. Further, there is insufficient guidance as to the function of said undisclosed nucleic acid molecule since the protein encoded by said nucleic acid merely contains 6 amino acids of SEQ ID NO: 2. Given the indefinite number of undisclosed

nucleic acid molecule, there is insufficient working example demonstrating all undisclosed nucleic acid molecules are effective for detecting all disease in a patient, let alone for treating, preventing and/or diagnosing all disease state in a subject.

Since the nucleic acid sequence of a polynucleotide determines its protein coding properties, predictability of which changes can be tolerated in a polynucleotide's nucleic acid sequence and still retain similar functions and properties requires a knowledge of, and guidance with regard to which nucleotide within the full-length nucleotide sequence, if any, are tolerant of modification and which are conserved or less tolerant to modification, and detailed knowledge of the ways in which the product's structure relates to its functional usefulness. Further, the transitional phrase "comprising" (claim 3) is open-ended. It expands the nucleic acid molecule to include additional nucleotides at either or both ends in addition to the polynucleotide 25-429 of SEQ ID NO: 1. Given the indefinite number of the additional nucleotides that may encompassed in the nucleic acid molecule of the instant claims, it is unpredictable which undisclosed polynucleotide will have the same structure and functions as the polynucleotide comprising SEQ ID NO: 1 that encodes SEQ ID NO: 2, in turn, would be useful for detecting allergic hypersensitivity in a patient.

With regard to nucleic acid molecule that encodes a protein that exhibits at least about 35% amino acid sequence identity to SEQ ID NO: 2 (claim 1), a "35% identity" means a 65% difference in amino acid sequence. There is insufficient guidance as to which amino acids within the full length polypeptide of SEQ ID NO: 2, the corresponding polynucleotide, to be substituted, deleted, or added and whether the resulting polypeptide encoded by the undisclosed nucleic acid molecule maintains its structure and function.

It is known in the art that the relationship between the amino acid sequence of a protein (polypeptide) and its tertiary structure (i.e. its binding activity) are not well understood and are not predictable (see Ngo et al., in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz, et al., (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495).

Skolnick *et al* teach that sequence-based methods for function prediction are inadequate and knowing a protein's structure does not tell one its function (See abstract, in particular).

Attwood *et al* teach that protein function is context-dependent and the state of the art of making functional assignments merely on the basis of some degree of similarity between sequences and the current structure prediction methods is unreliable (See figure, entire document).

Given the indefinite number of nucleic acid molecule, it is unpredictable which undisclosed nucleic acid molecule encodes a protein that has at least about 35% sequence identity or at least 65% difference to SEQ ID NO: 2 would have the same function as SEQ ID NO: 2. Until the function of the undisclosed nucleic acid molecule has been identified, it would take undue experimentation even for one skilled in the art to make and use the claimed nucleic acid molecule.

With regard to nucleic acid molecule which hybridizes to the complement of a nucleic acid molecule comprising SEQ ID NO: 1 or any nucleic acid molecule that encodes the amino acid sequence of SEQ ID NO: 2, there is insufficient guidance with respect to the length of the nucleic acid molecule without the nucleotide sequence that hybridizes to said complement or said nucleic acid molecule that encodes the amino acid sequence of SEQ ID NO: 2, and whether said nucleic acid molecule has the same function as SEQ ID NO: 1. Further, there is insufficient guidance about the specific hybridization condition used by applicant.

The state of the prior art as exemplified by Wallace *et al* is such that determining the specificity of hybridization probes is empirical by nature and the effect of mismatches within an oligonucleotide probe is unpredictable. Even if the probe is a 20mer, the total number of hits in a database search was 143,797,728, which suggest that some of the probes encompassed by the claims would not preferentially hybridize to the complement of SEQ ID NO: 1. Since the nucleic acid molecule mentioned above is not enabled, it follows that any vector, host cell and composition comprising said nucleic acid molecule are not enabled.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992). In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

7. Claims 1, 3, 23-29 and 49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of *any* isolated nucleic acid molecule that encodes any fragment of "at least 6 amino acids" of SEQ ID NO: 2, any nucleic acid molecule which "hybridizes" to the complement of a nucleic acid molecule comprising SEQ ID NO: 1, any isolated nucleic acid molecule which "hybridizes" to the complement of any nucleic acid molecule that encodes the amino acid sequence of SEQ ID NO: 2, any isolated nucleic acid molecule that encodes any protein that exhibits "at least about 35% amino acid sequence identity" to SEQ ID NO: 2, and any isolated nucleic acid molecule "comprises" nucleotides 25-249 of SEQ ID NO: 1.

The specification discloses only an isolated nucleic acid molecule comprising SEQ ID NO: 1 that encodes the amino acid sequence of SEQ ID NO: 2, a vector and an isolated host cell comprising said nucleic acid molecule for producing said polypeptide. The specification further discloses that a change in the expression levels of said nucleic acid molecule is associated with allergic hypersensitivity in a patient. The specification discloses overexpression of polynucleotide reduces the release of degranulation as determined by marker β hexoseaminidase, decreases the release of PGD2, LTC4, and GM-CSF 18 hours after mast cell activation.

With the exception of the specific nucleic acid molecule comprising SEQ ID NO: 1 for detection of allergic hypersensitivity in a patient, there is inadequate written description about the structure associated with function of all nucleic acid molecule mentioned above without the nucleotide sequence. Further, not all nucleic acid molecule that encodes a protein merely 6 amino acids of SEQ ID NO: 2 has the same function as SEQ ID NO: 2. Even if the nucleic acid molecule encodes a fragment of at least 6 amino acids, there is insufficient written description about which particular 6 amino acids of SEQ ID NO: 2, and the corresponding polynucleotide are part of the undisclosed nucleic acid molecule. The rest of the nucleic acid is not adequately described. With regard to claim 3, the transitional phrase "comprising" is open-ended. It expands the undisclosed nucleic acid molecule to include additional nucleotides at either or both ends in addition to the polynucleotide 25-429 of SEQ ID NO: 1. Without the nucleic acid, the claimed nucleic acid molecule is not adequately described.

With regard to nucleic acid molecule that encodes a protein that exhibits at least about 35% amino acid sequence identity to SEQ ID NO: 2 (claim 1), a "35% identity" means a 75% difference in amino acid sequence. There is inadequate written about which amino acids within the full length polypeptide of SEQ ID NO: 2, the corresponding polynucleotide to be substituted, deleted, or added and whether the resulting polypeptide maintains the same structure and function as SEQ ID NO: 2. Further, a 35% identity means 65% differences. Without the nucleic acid, the rest of the nucleic acid molecule is not adequately described.

With regard to nucleic acid molecule which hybridizes to the complement of a nucleic acid molecule comprising SEQ ID NO: 1 or any nucleic acid molecule that encodes the amino acid sequence of SEQ ID NO: 2 (claim 1), there is insufficient written description about the length of the nucleic acid molecule without the nucleotide sequence that hybridizes to the complement of the nucleic acid molecule that encodes the amino acid sequence of SEQ ID NO: 2, and whether said nucleic acid molecule has the same function as SEQ ID NO: 1. Further, the hybridization condition is not recited in the claim.

Given the lack of an additional nucleic acid molecule such as nucleic acid molecule that encodes a protein that exhibits at least about 35% amino acid sequence identity to SEQ ID NO: 2 as encompassed by the claims, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398; University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CA FC2004).*

Applicant is directed to the Final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

9. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The "isolated nucleic acid molecule which hybridizes to the complement of a nucleic acid molecule comprising SEQ ID NO: 1" and the "isolated nucleic acid molecule which hybridizes to the complement of a nucleic acid molecule that encodes the amino acid sequence of SEQ ID NO: 2" in claim 1 is ambiguous and indefinite because the specific hybridization condition such as the one disclosed on page 18 is not recited in the claim. One of ordinary skill in the art cannot appraise the metes and bound of the claimed invention.

10. The filing date of the instant claims 1-5, and 23-29 is deemed to be the filing date of the provisional application 60/279,115 filed 3/28/01, as the other provisional application 60/275,479 filed 3/14/01 and 60/251,835 filed 12/08/00 is drawn to a completely different nucleotides, and thus does not support the claimed limitations of polynucleotide encodes the amino acid sequence of SEQ ID NO: 2 of the instant application.

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claim 1 is rejected under 35 U.S.C. 102(a) as being anticipated by Waterston *et al* (Accession No AC 074365, Sept 2000; PTO 892).

Waterston *et al* teaches an isolated nucleic acid molecule that encodes a fragment of 80 amino acids of claimed SEQ ID NO: 2, which is at least 6 amino acids of SEQ ID NO: 2 (See enclosed sequence alignment, in particular). Thus, the reference teachings anticipate the claimed invention.

13. Claims 3 and 5 are rejected under 35 U.S.C. 102(a) as being anticipated by Accession No BF242113 (Nov 14, 2000; PTO 892).

The EST database teaches an isolated polynucleotide molecule comprises a nucleotide sequence that includes the claimed nucleotide 25-429 of SEQ ID NO: 1 (See enclosed sequence alignment, in particular). The term "comprises" is open-ended. It expands the claimed nucleotide 25-429 of SEQ ID NO: 1 to include additional nucleotide at either or both ends to include the reference nucleotide. Thus, the reference teachings anticipate the claimed invention.

14. Claims 1, 23-29 and 49 is rejected under 35 U.S.C. 102(b) as being anticipated by Dalton *et al* (Accession No M85165, Cell 68(3): 597-612, Feb 1992; PTO 892) and Dalton *et al*, Erratum in Cell 76(2): 411 (Jan 28, 1994; PTO 892).

Dalton et al teach isolated nucleic acid molecule such as Homo sapiens SRF accessory protein 1A (SAP-1) that has a stretch of "AAATGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA" from nucleotide 1878 to 1926 of the reference nucleotide (See enclosed sequence alignment, page 604, sequence, in particular). The reference nucleic acid molecule is identical to the nucleotides 3714 to 3762 of the claimed SEQ ID NO: 1 and inherently hybridizes to the complement of the claimed SEQ ID NO: 1 that has a stretch of nucleotides TTTACTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT from nucleotide 3714 to 3762 of claimed SEQ ID NO: 1. The reference further teaches the reference nucleic acid is operably linked to expression control elements such as GAL1-10/CYC1 promoter, vector comprising the reference nucleic acid molecule and host cell such as eukaryotic yeast cell or prokaryotic E coli (page 610, column 1, 3rd paragraph, in particular), comprising the reference vector for a method of producing the reference protein (See Experimental procedures on page 609, column 1, in particular). Dalton et al teach a composition comprising the reference nucleic acid and an aqueous carrier such as lithium acetate (See page 610, column 1, Yeast Transformation, in particular). Thus, the reference teachings anticipate the claimed invention.

15. Claims 2 and 4 are free of prior art.

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (703) 872-9306.

18. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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